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PATENT & TRADEMARK OFFICE

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	**Sinan Tas and Oktay Avci**
Application No.:	**10/682662**
Filed:	**October 9, 2003**
For:	**USE OF CYCLOPAMINE IN THE TREATMENT OF PSORIASIS**
Group Art Unit:	**1614**

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Docket No.: M67.2I-11334-US01

TRANSMITTAL LETTER

1. In regard to the above-identified application, in addition to this **1** page transmittal letter, we are submitting the attached:
4 page Supplemental Information Disclosure Statement; 3 page form listing cited references; copy of 40 references and Postcard.

2. With respect to fees:
   - ☒ No additional fee is required.
   - ☐ Attached is check(s) in the amount of $
   - ☐ Charge additional fee to our Deposit Account No. 22-0350.

3. **CONDITIONAL PETITION FOR EXTENSION OF TIME**
This conditional petition is being filed along with the papers identified in Item 1 above and provides for the possibility that Applicant has inadvertently overlooked the need for a petition and fee for extension of time or for a petition and fee for any other matter petitionable to the Commissioner as required. If any extension of time for the accompanying response is required or if a petition for any other matter is required, by petitioner, Applicant requests that this be considered a petition therefor.

4. Notwithstanding paragraph 2 above, if any additional fees associated with this communication are required and have not otherwise been paid, including any fee associated with the Conditional Petition for Extension of Time, or any request in the accompanying papers for action which requires a fee as a petition to the Commissioner, please charge the additional fees to Deposit Account No. 22-0350. Please charge any additional fees or credit overpayment associated with this communication to the Deposit Account No. 22-0350.

Respectfully submitted,

VIDAS, ARRETT & STEINKRAUS

Date: October 15 2004

By:
Walter J. Steinkraus
Registration No.: 29592

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Certificate Under 37 CFR 1.8: I hereby certify that this Transmittal Letter and the paper(s) as described herein, are being deposited in the U.S. Postal Service, as FIRST CLASS MAIL, addressed to Mail Stop Amendment, Commissioner for Patent, P.O. Box 1450, Alexandria, VA 22313-1450, on October 15, 2004.

Rebecca M Painschab
Rebecca M. Painschab

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SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

Listed below or on an attached form listing the cited references and/or a copy of a PTO-892 form is information known to applicant(s). A copy of each listed publication, U.S. patent, foreign patent and U.S. patent application is being submitted herewith, along with a concise explanation of information in a foreign language, if any, pursuant to 37 C.F.R. §1.97-1.98, ***except that*** U.S. applications from which priority is claimed under 35 U.S.C. §120, and documents cited in such priority applications, may be omitted from the enclosures pursuant to 37 C.F.R. 1.98(d). Applicant's submission of copies of U.S. applications does not constitute a waiver of the confidentiality of such applications. As such, **Applicant requests that any copies of unpublished US applications submitted herewith be excluded from the file wrapper pursuant to 37 C.F.R. §1.14.**

Applicants respectfully request that the listed information be considered by the Examiner and be made of record in the above-identified application. If the form listing the cited references or PTO-892 from a prior application is enclosed, the Examiner is requested to initial and return it in accordance with MPEP §609.

This statement is not intended to represent that a search has been made or that the information cited in the statement is prior art, or is or is considered to be, material to patentability as defined in §1.56.

Applications that are listed on the accompanying form listing the cited references as related by priority are related by priority claim under 35 USC §120. Pursuant to 37 CFR §1.98(d), no copies of cited art in a previous application(s) to which priority was claimed need be submitted. Applicant is providing copies of the form listing the cited references and/or 892 forms from these cases.

_X_ **I.** This statement qualifies as a no-fee Information Disclosure Statement under *37 C.F.R. §1.97(b)* or otherwise because to the knowledge of the undersigned attorney it is being filed (check all that apply):

_____ (1) within 3 months of the filing date of the application (other than a CPA); or
_____ (2) within 3 months of entry of the national stage; or
_X_ (3) before the mailing of a first Office Action on the merits;
_____ (4) before the mailing of a first Office Action after the filing of a request for continued examination (RCE) under §1.114;
_____ (5) as part of a continued prosecution application (CPA); or
_____ (6) during the period of a suspension of action for a CPA under 37 C.F.R. §1.103(b).

_____ **II.** This statement is believed to require a fee or the submission of a certification under *37 C.F.R. §1.97 (c)* or otherwise. If this statement is being filed after the latest of: (1) three months beyond the filing date of a national application (other than CPA); (2) three months beyond the date of entry of the national stage as set forth in §1.491 in an international application; (3) the mailing of a first Office Action on the merits; (4) the mailing of a first Office Action after the filing of a request for continued examination under §1.114; or (5) after the filing of a request for a continued prosecution application, but before the mailing date of the earlier of a final office action under §1.113, a notice of allowance under §1.311 or an action that otherwise closes prosecution in the application, then:

_____ (1) a certification as specified in §1.97(e) is provided below; or
_____(2) a fee of $180.00 as set forth in §1.17(p) is authorized below, enclosed, or included with the payment of other papers filed together with this statement.

_____ **III.** *37 C.F.R. §1.97(d).* If this statement is being filed after the mailing date of the earlier of a final office action under §1.113, a notice of allowance under §1.311, or an action that otherwise closes prosecution in the application, but before payment of the issue fee, then:

_____ (1) a certification as specified in §1.97(e) is completed below; and

______(2) a fee of $180.00 as set forth in §1.17(p) is authorized below, enclosed, or included with payment of other papers filed together with this statement.

_X_ **IV.** *Fee Authorization.* If any fee is due for consideration of this Information Disclosure Statement and full payment has not been submitted herewith, regardless of which boxes have been checked above, the Commissioner is hereby authorized to charge any additional fees associated with this communication to Deposit Account No. 22-0350. The Commissioner is hereby authorized to credit any overpayment associated with this communication to Deposit Account No. 22-0350.

If paragraph II.1 or III is checked, also check one of the paragraphs below

_____ I hereby certify, under 37 CFR §1.97(e)(1), that each item of information contained in this Information Disclosure Statement was first cited in a communication from a foreign patent office in a counterpart foreign application not more than three months prior to the date of the filing of this information disclosure statement.

______ This communication was not received by any individual designated in § 1.56(c) more than thirty days prior to the filing of the Information Disclosure Statement.

_____ I hereby certify, under 37 CFR §1.97(e)(2), that no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and to the knowledge of the person signing the statement after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 1.56(c) more than three months prior to the filing of the Information Disclosure Statement.

For the purpose of this certification, Applicant considers the PCT International Search Authority to constitute a foreign patent office.

If this Supplemental Information Disclosure Statement has been submitted without the appropriate box checked, Applicant requests that this Supplemental Information Disclosure Statement be considered nevertheless if it is timely submitted under any of the provisions of 37 C.F.R. §1.97 or otherwise. Finally, if any petition is necessary to ensure consideration of this Supplemental Information Disclosure Statement, Applicant requests that this be treated as such a petition.

Respectfully submitted,

VIDAS, ARRETT & STEINKRAUS

Date: October 15, 2004

By:
Walter J. Steinkraus
Registration No.: 29592

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LIST OF PATENTS AND PUBLICATIONS FOR APPLICANT'S INFORMATION DISCLOSURE STATEMENT **(Use several sheets if necessary)**	**ATTY DOCKET NO.:** M67.2I-11334-US01	**APPLICATION NO.:** 10/682662
	APPLICANT: Sinan Tas and Oktay Avci	
	FILING DATE: October 9, 2003	**GROUP:** 1614

OTHER ART (Including Author, Title, Date, Pertinent Pages, Ect.)

	CA		Levine, Edward M. et al., "Sonic Hedgehog Promotes Rod Photoreceptor Differentiation in Mammalian Retinal Cells *In Vitro*,' *The Journal of Neuroscience*, August 15, 1997, 17(16):6277-6288.
	CB		Kim, Seung K. et al., "Pancreas development is promoted by cyclopamine, a Hedgehog signaling inhibitor," *Proc. Natl. Acad. Sci. USA*, Vol. 95, pp. 13036-13041, October 1998, Developmental Biology.
	CC		Incardona, John P. et al., "The teratogenic *Veratrum* alkaloid cyclopamine inhibits Sonic hedgehog signal transduction," *Development 125*, pp. 3553-3562 (1998), Printed in Great Britain © The Company of Biologists Limited 1998.
	CD		Cooper, Michael K., "Teratogen-Mediated Inhibition of Target Tissue Responses to Shh Signaling," www.sciencemag.org, *SCIENCE*, Vol. 280, pp. 1603-1607 (5 June 1998).
	CE		Berman, David M. et al., "Inhibition of Prostate Morphogenesis by the Sonic Hedgehog Pathway Inhibitor Cyclopamine," *The Journal of Urology*, Vol. 163, No. 4, Supplement, p. 204 (Tuesday, May 2).
	CF		Stenkamp, Deborah L., "Function for *Hedgehog* Genes in Zebrafish Retinal Development," **Developmental Biology**, Volume 220, pp. 238-252 (2000).
	CG		Treier, Mathias et al., "Hedgehog signaling is required for pituitary gland development," *Development 128*, pp. 377-386 (2001), Printed in Great Britain © The Company of Biologists Limited 2001.
	CH		Kahane, Nitza et al., "The third wave of myotome colonization by mitotically competent progenitors: regulating the balance between differentiation and proliferation during muscle development," *Development 128*, pp. 2187-2198 (2001), Printed in Great Britain © The Company of Biologists Limited 2001.
	CI		Fan, Hongran et al., "Sonic Hedgehog Opposes Epithelial Cell Cycle Arrest," *The Journal of Cell Biology*, Volume 147, Number 1, October 4, 1999, pp.71-76.
	CJ		Sukegawa, Akiko et al., "The concentric structure of the developing gut is regulated by Sonic hedgehog derived from endodermal epithelium," *Development 127*, pp. 1971-1890 (2000), Printed in Great Britain © The Company of Biologists Limited 2000.
	CK		Ramalho-Santos, Miguel et al., "Hedgehog signals regulate multiple aspects of gastrointestinal development," *Development 127*, pp. 2763-2772 (2000), Printed in Great Britain © The Company of Biologists Limited 2000.
	CL		Zhang, Jian et al., "Downregulation of Hedgehog Signaling Is Required for Organogenesis of the Small Intestine in *Xenopus*," *Developmental Biology*, Volume 229, pp. 188-202 (2001).
	CM		Van Den Brink, Gus R. et al., "Sonic Hedgehog Regulates Gastric Gland Morphogenesis in Man and Mouse," *Gastroenterology*, Volume 121, pp. 317-328 (2001).

EXAMINER	**DATE CONSIDERED**

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

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	CA		Ishizuya-Oka, Atsuko et al., "Thyroid hormone-induced expression of Sonic hedgehog correlates with adult epithelial development during remodeling of the Xenopus stomach and intestine," *Differentiation*, Volume 69, pp. 27-37 (2001)
	CB		van den Brink, G.R. et al., "Sonic hedgehog expression correlates with fundic gland differentiation in the adult gastrointestinal tract," *Gut*, Volume 51, pp. 628-633 (2002).
	CC		Perron, Muriel et al., "A novel function for *Hedgehog* signaling in retinal pigment epithelium differentiation," *Development 130*, Volume 130, pp. 1565-1577, © 2003 The Company of Biologists Ltd.
	CD		Watkins, D. Neil et al., "Hedgehog signaling within airway epithelial progenitors and in small-cell lung cancer," *NATURE*, Volume 422, pp. 313-317 (20 March 2003) © 2003 Nature Publishing Group.
	CE		Stenkamp, Deborah L., "Extraretinal and retinal hedgehog signaling sequentially regulate retinal differentiation in zebrafish," *Departmental Biology*, Volume 258, pp. 349-363 (2003) © 2003 Elsevier Science (USA).
	CF		Niemann, C. et al., "Indian hedgehog and ß-catenin signaling: Role in the sebaceous lineage of normal and neoplastic mammalian epidermis," *PNAS*, Volume 100, Supplement 1, pp. 11873-11880 (September 30, 2003).
	CG		Jarov, Artem et al., "A dual role for Sonic hedgehog in regulating adhesion and differentiation of neuroepithelial cells," *Developmental Biology*, Volume 261, pp. 520-536 (2003) © 2003 Elsevier Inc.
	CH		Allen, Mary et al., "Hedgehog Signaling Regulates Sebaceous Gland Development," *American Journal of Pathology*, Volume 163, No. 6, pp. 2173-2178 (6 December 2003) Copyright © American Society for Investigative Pathology.
	CI		Yao, Humphrey Hung-Chang et al., "Desert Hedgehog/Patched 1 signaling specifies fetal Leydig cell fate in testis organogenesis," *GENES & DEVELOPMENT*, Volume 16, pp. 1433-1440 © 2002 by Cold Spring Harbor Laboratory Press.
	CJ		Wang, Bu-er et al., "Inhibition of Epithelial Ductal Branching in the Prostate by Sonic Hedgehog Is Indirectly Mediated by Stromal Cells," *The Journal of Biological Chemistry*, Volume 278, No. 20, pp. 18506-18513 (May 16, 2003) © 2003 by the American Society for Biochemistry and Molecular Biology, Inc.
	CK		Freestone, Sarah H. et al., "*Sonic hedgehog* regulates prostatic growth and epithelial differentiation," *Developmental Biology*, Volume 264, pp. 352-362 (2003).
	CL		Berman, David M. et al. "Widespread requirement for Hedgehog ligand stimulation in growth of digestive tract tumours," *NATURE*, Volume 425, pp. 846-851 (23 October 2003).
	CM		Grachtchouk, Vladimir et al., "The magnitude of hedgehog signaling activity defines skin tumor phenotype," *The EMBO Journal*, Volume 22, No. 11, pp. 2741-2751 (2003)

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	CA		Zhang, Yan et al., "Hedgehog acts as a somatic stem cell factor in the *Drosophila* ovary," *NATURE*, Volume 410, pp. 599-604 (29 March 2001) © 2001 Macmillan Magazines Ltd.
	CB		Outram, Susan V. et al., "Hedgehog Signaling Regulates Differentiation from Double-Negative to Double-Positive Thymocyte," *Immunity*, Volume 13, pp. 187-197 (August 2000) Copyright © 2000 by Cell Press.
	CC		Keeler, Richard F., "Teratogenic Effects of Cyclopamine and Jervine in Rats, Mice and Hamsters," *PROCEEDINGS OF THE SOCIETY FOR EXPERIMANTAL BIOLOGY AND MEDICINE*, Volume 149, pp. 302-306 (1975) Copyright © 1975 by the Society for Experimental Biology and Medicine.
	CD		Keller, R.F., "Teratogenic Compounds of *Veratrum Californicum* (Durand)-VI. The Structure of Cyclopamine," *Phytochemistry*, Volume 8, pp. 223-225 (1969).
	CE		Omnell, M.L. et al., "Expression of *Veratrum* Alkaloid Teratogenicity in the Mouse," *TERATOLOGY*, Volume 105-119 (1990).
	CF		Talpale Jussi et al., "Effects of oncogenic mutations in *Smoothened* and *Patched* can be reversed by cyclopamine," *NATURE*, Volume 406, pp. 1005-1009 (31 August 2000) © 2000 Macmillan Magazines Ltd.
	CG		Detmer, Kristina et al., "Erythroid Differentiation *in Vitro* Is Blocked by Cyclopamine, an Inhibitor of Hedgehog Signaling," *Blood Cells, Molecules, and Diseases*, Volume 26, No. 4, pp. 360-372 (2000) Copyright © 2000 by Academic Press.
	CH		Michimukai, Eiji et al., "Mutations in the Human Homologue of the *Drosophila* Segment Polarity Gene *Patched* in Oral Squamous Cell Carcinoma Cell Lines," *In Vitro Cellular & Developmental Biology*, Volume 37, No. 7, pp.459-464 (Jul/Aug 2001) ProQuest Medical Library.
	CI		Berman, David M. et al., "Medulloblastoma Growth Inhibition by Hedgehog Pathway Blockade," *SCIENCE*, Volume 297, pp. 1559-1561 (30 August 2002).
	CJ		Watkins, D. Neil et al., "Hedgehog signaling within airway epithelial progenitors and in small-cell lung cancer," *NATURE*, Volume 422, pp. 313-317 (20 March 2003) ©2003 Nature Publishing Group.
	CK		Thayer, Sarah P. et al., "Hedgehog is an early and late mediator of pancreatic cancer tumorigenesis," *NATURE*, Volume 425, pp. 851-856 (23 October 2003).
	CL		Qualtrough, David et al., "Hedgehog Signalling in Colorectal Tumour Cells: Induction of Apoptosis with Cyclopamine Treatment," *Int. J. Cancer*, Volume 110, pp. 831-837 (2004) © 2004 Wiley-Liss, Inc.
	CM		Cooper, Michael K. et al., "Teratogen-Mediated Inhibition of Target Tissue Response to Shh Signaling," *SCIENCE*, Volume 280, pp. 1603-1607 (5 June 1998).
	CN		Detmer, Kristina et al., "Erythroid Differentiation *in Vitro* Is Blocked by Cyclopamine, an Inhibitor of Hedgehog Signaling," *Blood Cells, Molecules, and Diseases*, Volume 26, No. 4, pp. 360-372 (August) Copyright © 2000 by Academic Press.

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